MARKED-UP COPY OF AMENDED CLAIMS:

Please amend claim 17 as follows:

17. (Amended) The method [solid pharmaceutical dosage form] of claim 37, [14] further comprising a non-effervescent disintegration agent.

REMARKS

Claim 14-21 are pending in the present application. In the Office Action of September 25, 2002, claims 14-15 and 17-21 have been rejected under 35 U.S.C. § 102 (b) as allegedly obvious over U.S. Patent No. 6,117,912 to DiSanto ("*DiSanto*"). Claims 14-21 also have been rejected under 35 U.S.C. § 103 (a) as allegedly obvious over *DiSanto* in view of U.S. Patent No. 3,972,995 to Tsuk et al. ("*Tsuk*").

By this Amendment, Applicants have cancelled claims 14-16 and 18-21, amended claim 17, and added new claims 22-81, which together with the remarks set forth below place the present application in condition for allowance. Entry of the amended and new claims, reconsideration and allowance of all pending claims are respectfully requested.

I. INVENTION, *DISANTO* AND *TSUK*

The Examiner rejected claims 14-15 and 17-21 as allegedly anticipated by *DiSanto*, pointing to Example 3 of *DiSanto* that allegedly "teaches an effervescent selegiline tablet for sublingual or buccal administration."

The Examiner also has rejected claims 14-21 as obvious over *DiSanto* in view of *Tsuk*. This rejection appears primarily directed to claim 16, which recites a dosage form containing a bioadhesive. According to the Examiner, *Tsuk* teaches a buccal dosage form that "contains a moisture-activated adhesive precursor."

Referring to *DiSanto*, Example 3 appears to disclose a sublingual selegiline tablet that includes an effervescent pair. *DiSanto* does not provide a reason for formulating selegiline with an effervescent pair. *DiSanto* provides no other disclosure concerning effervescence, or any disclosure at all about additional components for effervescent formulations of selegiline. *Tsuk* teaches a dosage form for buccal administration that includes moisture activated adhesive precursor. *Tsuk* does not disclose effervescent agents.

Applicants canceled the rejected independent claim 14. New independent claims 22, 30, 37, 54, 64, and 71 were added. Applicants assert that these independent claims and the claims dependent therefrom are neither anticipated by nor obvious over *DiSanto*, alone or in combination with *Tsuk*.

II. NEW CLAIMS 22, 30, 37, 54, 64, AND 71

A. New claim 22 in view of DiSanto, alone or in combination with Tsuk.

New claim 22 recites a dosage form that includes a medicament and an effervescent agent "present in an amount between about 5% by weight and about 80% by weight." New claim 22 is supported in the application as filed. *See, e.g.*, Specification, at page 5, lines 3-7. *DiSanto* does not teach the inclusion of an effervescent agent in the recited amount. Furthermore, *DiSanto* provides no motivation for one skilled in the art to modify the amount of the effervescent components in the tablet of the *DiSanto* Example 3 in the direction of the recited range. In fact, *DiSanto* contains no discussion whatsoever regarding the function of the effervescent components or amounts thereof. *Tsuk* does not discuss effervescence at all. Thus, Applicants respectfully maintain that claim 22 and claims dependent therefrom are neither anticipated by nor obvious in view of *DiSanto*, alone or in combination with *Tsuk*.

B. New claim 30 in view of DiSanto, alone or in combination with Tsuk.

New claim 30 recites a dosage form that includes a medicament, an effervescent agent, and "*one or more glidants, lubricants, binders, sweeteners, non-effervescent disintegration agents, flavoring or coloring components.*" New claim 30 is supported in the application as filed. *See, e.g.*, Specification, at page 12, lines 3-9. Neither *DiSanto* nor *Tsuk* teaches or suggests the inclusion of the recited components in the dosage form containing an effervescent agent. Thus, Applicants respectfully maintain that claim 30 and claims dependent therefrom are neither anticipated by nor obvious in view of *DiSanto*, alone or in combination with *Tsuk*.

C. New claim 37 in view of DiSanto, alone or in combination with Tsuk.

New claim 37 recites a method of administering at least one systemically distributable pharmaceutical agent across the oral mucosa by providing a solid dosage form that includes a medicament, an effervescent agent, and "at least one pH adjusting substance *in amount additional to the amount required for effervescence, said amount being tolerable to the subject, wherein said pH adjusting substance and said amount thereof are selected to alter pH of a local environment of said medicament to control the relative concentrations of ionized and unionized forms of said medicament*," and placing and holding the dosage form in the mouth of the patient "*wherein said at least one effervescent agent promotes absorption of said orally administerable medicament across the oral mucosa.*" New claim 37 is supported in the application as filed. *See, e.g.*, Specification, page 7, line 20 to page 8, line 10; at page 9, lines 9-11; at page 5, lines 1-3. *DiSanto* does not teach or suggest the inclusion of a pH-adjusting substance to alter

the local environment of the medicament in order to "*control the relative concentrations of ionized and unionized forms of said medicament.*" Furthermore, *DiSanto* neither discloses nor suggests that effervescence may be effective in promoting penetration across the oral mucose. Thus, Applicants respectfully maintain that claim 37 and claims dependent therefrom are neither anticipated by nor obvious in view of *DiSanto*.

D. New claim 54 in view of DiSanto.

New claim 54 recites a method of administering at least one systemically distributable pharmaceutical agent across the oral mucosa by providing a solid dosage form that includes a medicament and an effervescent agent "*present in the amount between about 5% by weight and about 80% by weight,*" and placing and holding the dosage form in the mouth of the patient "*wherein said at least one effervescent agent promotes absorption of said orally administerable medicament across the oral mucosa.*" New claim 54 is supported in the application as filed. *See, e.g.*, Specification, at page 5, lines 3-7; at page 9, lines 9-11; at page 5, lines 1-3. *DiSanto* does not disclose a dosage form containing an effervescent agent in the recited range. Furthermore, Example 3 of *DiSanto* merely discloses the content of a dosage form, without any discussion whatsoever regarding the reason for the effervescent formulation, the use of effervescence in promoting penetration across the oral mucosa in addition to disintegration or the preferred amounts of the effervescent agent useful for accomplished the same. Thus, *DiSanto* provides no motivation for one skilled in the art to arrive at the invention recited in new claim 54. On these bases, Applicants respectfully maintain that claim 54 and claims dependent therefrom are neither anticipated by nor obvious in view of *DiSanto*.

E. New claim 64 in view of DiSanto.

New claim 64 recites a method of manufacturing a solid pharmaceutical dosage form for oral administration across the oral mucosa, the method including mixing a medicament, a pH adjusting substance, and an effervescent agent "*present in the amount between about 5% by weight and about 80% by weight,*" and using the mixture to produce the dosage form. New claim 73 is supported in the application as filed. *See, e.g.*, Specification, at page 10. *DiSanto* does not disclose a dosage form containing an effervescent agent in the recited range. Example 3 of *DiSanto* lacks discussion regarding the reason for formulating the dosage form with an effervescent agent or the preferred amount of the effervescent agent. Thus, *DiSanto* provides no motivation for one skilled in the art to arrive at the invention recited in new claim 64. On these bases, Applicants respectfully maintain that claim 64 and claims dependent therefrom are neither anticipated by nor obvious in view of *DiSanto*.

F. New claim 71 in view of DiSanto

New claim 71 recites a method of manufacturing a solid pharmaceutical dosage form for oral administration across the oral mucosa, the method including mixing a medicament, an effervescent agent, and "at least one pH adjusting substance *in amount additional to the amount required for effervescence, said amount being tolerable to the subject, wherein said pH adjusting substance and said amount thereof are selected to alter pH of a local environment of said medicament to control the relative concentrations of ionized and unionized forms of said medicament*," and using the mixture to produce the dosage form. New claim 71 is supported in the application as filed. *See, e.g.*, Specification, page 7, line 20 to page 8, line 10; at page 9, lines 9-11; at page 5, lines 1-3. *DiSanto* does not teach or suggest the inclusion of a pH-adjusting substance to alter the local environment of the medicament in order to "*control the relative concentrations of ionized and unionized forms of said medicament.*" Furthermore, *DiSanto* neither discloses nor suggests that effervescence may be effective in promoting penetration across the oral mucosa. Thus, Applicants respectfully maintain that claim 71 and claims dependent therefrom are neither anticipated by nor obvious in view of *DiSanto*.

In view of the above claim amendments and foregoing remarks, it is believed that this application is now in condition for allowance. Reconsideration is respectfully requested. However, if the Examiner still believes that there are any objections to this application, he is encouraged to telephone the undersigned at (908) 654-5000.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

Respectfully submitted,

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